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# Dosimetric evaluation of inclusion of proximal seminal vesicle in target volume in low-risk prostate cancer treated with stereotactic body radiotherapy

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## ABSTRACT

**Aims**: Ultra hypofractionation using stereotactic body radiotherapy (SBRT) for low-risk PCa is considered a viable treatment option. The target volume for ultra hypofractionated RT was determined as prostate and/or proximal seminal vesicles; however, there are no clear guidelines on when to add a proximal seminal vesicle to the target volume. We aimed to dosimetrically assess the effect of inclusion of the proximal seminal vesicle in the planning target volume (PTV) on the dose distribution of organ at risk (OAR) when SBRT is administered to patients with low-risk PCa.

**Methods**: Low-risk PCa cases who underwent SBRT with CyberKnife were retrospectively screened, and 20 random cases were included. The contours of OARs and target volumes were checked as recommended in international contouring atlases by the same radiation oncologist. Two treatment plans by determining two different PTV (prostate alone in plan 1 and prostate with proximal seminal vesicles in plan 2) were made by the same specialist physicist. 5×7.25 Gy was chosen as the dose schedule defined for both plans.

**Results**: Regarding coverage, homogeneity index, and new conformity index (nCI), there was no significant difference between the two plans (p=0.397, p=0.452, p=0.225). The plan 2 had a greater PTV Dmax (p<0.001). There was better conformity index at plan 1, as well as lower monitor unit and beam on time (p<0.05). The plan 1 had statistically lower values for each treatment parameter assessed for bladder (p<0.05). The treatment parameters evaluated for the rectum were statistically lower in the plan 1, except for V32.625 (p<0.05). The plan 1 was statistically better in terms of V29.5 for the penile bulb and V37.5 and V38 for neurovascular bundles (p<0.05). There was no significant difference between the two plans in terms of femoral heads and bowel (p=0.180, p=0.209, p=0.398, p=0.726, p=0.053, p=0.068). In addition, regardless of plan type, a majority of treatment parameters for bladder were statistically significantly affected in plans with a PTV volume greater than 100 cc (p<0.05).

**Conclusion**: In low-risk PCa, inclusion of the proximal seminal vesicle in the target volume may be overlooked as quantitatively insignificant increases in high-dose OAR volumes as they do not exceed dose constraints in routine clinical practice, and these high-dose OAR volumes are likely to be important in the development of toxicity. We recommend that special attention be paid to the high doses exposed in OARs in low-risk PCa. In addition, it should be kept in mind that bladder toxicity may increase with increasing PTV volume, especially above 100 cc.

**Keywords**: Low-risk, prostate cancer, prostate, seminal vesicle, stereotactic body radiotherapy, target volume

## INTRODUCTION

Since radiotherapy (RT) has comparable results with surgical treatment in prostate cancer (PCa), it is an accepted treatment method in both low-, medium-, and high-risk groups.[1] RT techniques have changed considerably over the years with the development of RT devices, and these innovations have significantly affected the management of PCa. The effectiveness of conventional RT schemes, whose daily treatment dose varies between 1.8-2 Gy and the total number of fractions varies between 37-45, is still valid, and their use continues today.[2,3] The fact that PCa has a radiobiologically lower alpha-beta ratio than adjacent healthy organs has led to the hypothesis that treatment-related toxicity may be lower than conventional methods, which has been the main reason to evaluate the potential of hypofractionated RT schemes in PCa management.[3] In addition, since the total duration of treatment is reduced with hypofractionated treatments, it both increases the patient's compliance and provides economic gain.

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Hypofractionated RT refers to applications where the daily treatment dose is larger and the number of fractions is lower than with traditional techniques. Moderate hypofractionation (2.35-3.4 Gy daily doses, 20-28 fractions) and extreme hypofractionation (>6Gy daily doses, 4-7 fractions) are the hypofractionation schemes adopted worldwide.[4,5] Ultra hypofractionation using stereotactic body radiotherapy (SBRT) for low-risk PCa is considered a viable treatment option with promising oncologic outcomes.[5-7]

Regardless of the RT scheme, target volumes are defined for the prostate, seminal vesicle, and pelvic lymph nodes according to the risk group. The target volume for ultra hypofractionated RT was determined as prostate and/or proximal seminal vesicles; however, there are no clear guidelines on when to add a proximal seminal vesicle to the target volume.[6,7] The entire prostate is always included in the clinical target volume (CTV). Regarding the inclusion of the seminal vesicles in the CTV, different practice patterns exist. To avoid underdosing at the base of the prostate, some clinicians include the proximal seminal vesicles, regardless of risk group or magnetic resonance imaging findings. Others prefer to include seminal vesicles when involved or in higher risk patients. With the expansion of the irradiated volume, there may be an increase in undesirable doses in neighboring critical organs such as the bladder, rectum, penile bulb, and bowel. Despite the benefits of SBRT already described, steep dose gradients require careful evaluation of nearby normal tissues. Therefore, during the SBRT treatment planning process, it is crucial for clinicians to have proper information of the dose limitations about normal tissues.

Although SBRT studies for late toxicity data are still under development, we aimed to dosimetrically assess the effect of inclusion of the proximal seminal vesicle in the target volume on the dose distribution of surrounding organs when SBRT is administered to patients with low-risk PCa. In this context, we intend to compare the dosimetric variations between the two treatment plans by determining two different targets (prostate alone or prostate with proximal seminal vesicles) that include both scenarios by using planning computed tomography (pCT) taken during the treatment of patients receiving SBRT.

## METHODS

### Ethics

The study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective design, individual consent was not required. The study was initiated with the approval of the Samsun University Clinical Researches Ethics Committee (Date: 2023, Decision No: 6/10).

### Patient population

Low-risk PCa cases who underwent SBRT with CyberKnife between March 2017 and March 2023 in the Radiation Oncology Clinic of Samsun Training and Research Hospital were retrospectively screened, and 20 random cases were included in the study.

### Treatment

Four fiducial markers were implanted for image guidance in patients 1 week prior to simulation. All patients underwent pCT with a 1 mm slice thickness. During the simulation, they were instructed to have a comfortably full bladder and an empty rectum in the supine position with a knee wedge. Magnetic resonance imaging was performed and used for image fusion to contour target volumes and organ at risk (OAR). The planning target volume (PTV) was defined for the prostate in 11 patients and for the prostate and the proximal seminal vesicle in 9 patients. All patients recieved 35 Gy over five fractions.

### Re-contouring and re-planning

Our study was carried out on the pCT for SBRT of these patients whose treatment had been completed previously. For the dosimetric study, the patients were evaluated by the same radiation oncologist, and the contours of OARs (bladder, rectum, penile bulb, femoral heads, neurovascular bundles, and bowel) and target volumes were checked as recommended in international contouring atlases.[8-10] It has been re-contoured for those who do not comply with the definitions specified in the guidelines in order to meet the same standards. The bladder and rectum were delineated as the entire organ. The rectum was contoured from anal verge to recto-sigmoid flexure. PTV was determined by giving a margin of 5 mm from all directions and 2 mm from the posterior to the CTV created by defining the prostate alone in plan 1 and the prostate plus 1 cm of the proximal seminal vesicle in plan 2. For each patient, two different plans were made by the same specialist physicist (**Figure 1**). Since the most commonly used dose for PCa SBRT is 5×7.25 Gy, it was chosen as the dose schedule defined for both plans in our study.[11]

The normal tissue dose constraints in our institution were shown in **Table 1**.[12] For the dosimetric evaluation, in addition to the dose constraints used in our clinic, the following treatment parameters were examined for PTV and OARs. For PTV: Dmax, coverage, conformity index (CI), homogeneity index (HI), new conformity index (nCI), monitor unit (MU), beam on time; for bladder: Dmax, V37.5, V37, V18.125, D0.1 cc, D1 cc, D5 cc, D10 cc, and D15 cc; for rectum: Dmax, V36.25, V32.625, V29, V29, V18.125, V5, V10, and V20; for penile bulb: V29.5, V30; for femoral heads: V14.5 and Dmax; for neurovascular bundles: V37.5 and V38; for bowel: Dmax and V29.

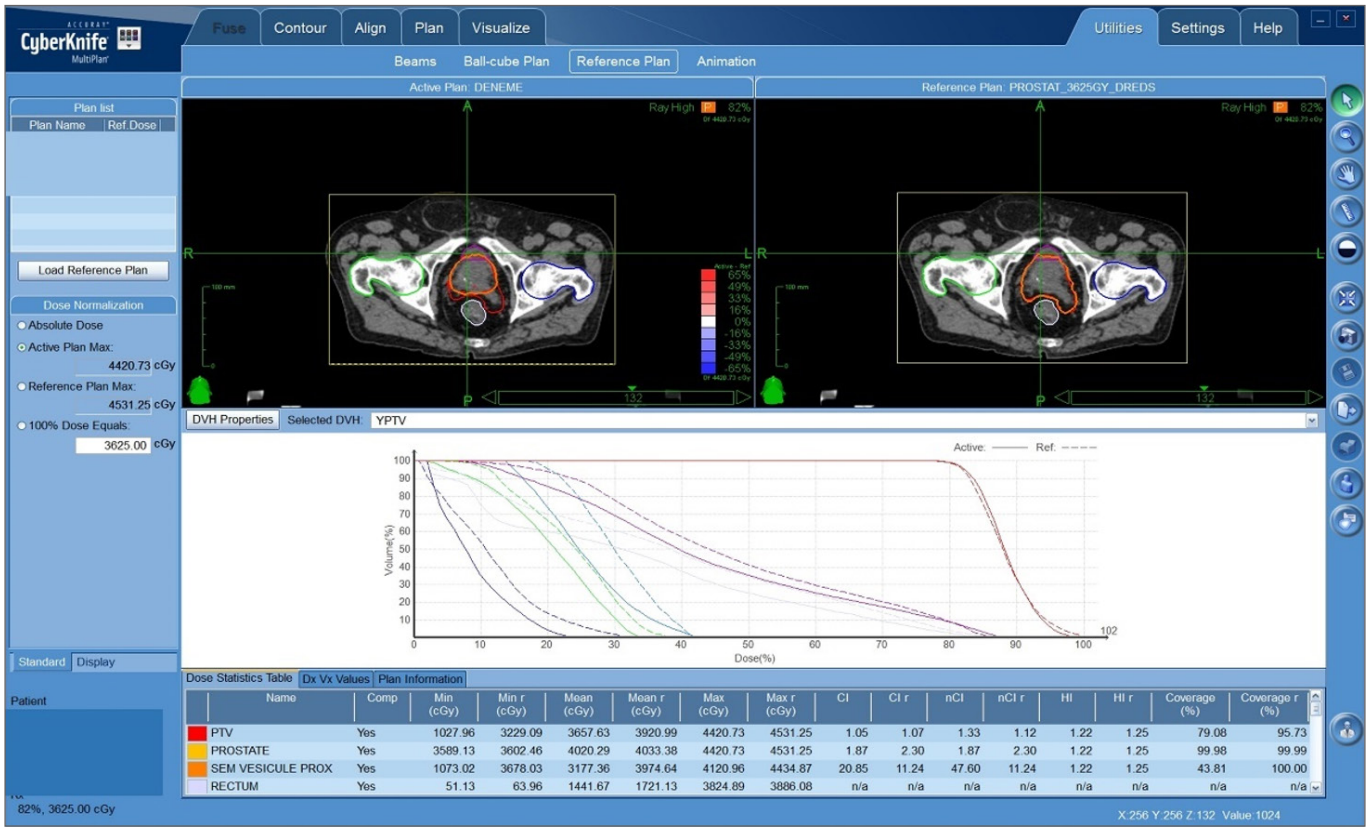


**Figure 1.** The dose distributions and dose-volume histograms of Plan 1 and Plan 2 for the same patient.

**Table 1.** Target volume and organs at risk dose constraints for treatment plans (36.25 Gy/5 fx)

| Structure | Dosimetric index | Acceptance criteria |
|---|---|---|
| CTV | Coverage | 100 % |
| PTV | Coverage<br>CI<br>HI | 95 %<br>≤1.2<br>≤1.2 |
| Bladder | Dmax<br>V37.5<br>V37 | 38 Gy<br>< 5 cm3<br>< 10 cm3 |
| Rectum | Dmax<br>V36.25<br>V32.625<br>V29<br>V18.125 | 38 Gy<br>< 5 %<br>< 10 %<br>< 20 %<br>< 50 % |
| Penile Bulb | V29.5<br>V30 | < 50 %<br>< 3 cc |
| LFH | Dmax<br>V14.5 | < 30 Gy<br>< 5 % |
| RFH | Dmax<br>V14.5 | < 30 Gy<br>< 5 % |
| Neurovascular bundles | V37.5<br>V38 | < 20 %<br>< 50 % |
| Bowel | Dmax<br>V24 | 25 Gy<br>< 1 cc |

CI: Conformity index; CTV: Clinical target volume; HI: Homogeneity index; LFH: Left femoral head; PTV: Planning target volume; RFH: Right femoral head

### Statistical Analysis

All parameters were expressed as mean and/or standard deviation. The two-sided paired t-test was used for normally distributed data and Wilcoxon Cox test for non-normally distributed data. SPSS v25 statistical program was used, p<0.05 was considered significant.

## RESULTS

A comparison of treatment parameters for PTV and each OAR for the two plans is shown in **Table 2**. Regarding coverage, HI and nCI, there was no significant difference between the two plans (p=0.397, p=0.452, p=0.225). The second plan had a greater PTV Dmax (p<0.001). There was better CI (p=0.007) at first plan, as well as lower MU (p=0.019) and beam on time (p=0.022).

The first plan had statistically lower values for each treatment parameter assessed for bladder (p<0.05). The treatment parameters evaluated for the rectum were statistically considerably lower in the first plan, except for V32.625 (p<0.05). The first plan was statistically better in terms of treatment parameters of V29.5 for the penile bulb (p=0.037) and V37.5 and V38 for neurovascular bundles (p<0.001, p=0.047). There was no significant difference between the two plans in terms of femoral heads and bowel (p=0.180, p=0.209, p=0.398, p=0.726, p=0.053, p=0.068).

In addition, regardless of plan type, a majority of treatment parameters for bladder and femoral head Dmax values were statistically significantly affected in plans with a PTV volume greater than 100 cc (p<0.05, **Table 3**). There was no difference for target and other OARs parameters with increasing target volume.

**Table 2.** Dosimetric comparisons of target volume and organs at risk doses for Plan 1 and 2

| Structure | Dosimetric index | Acceptance criteria | Plan 1 (Prostate) | | Plan 2 (Prostate+Proximal Seminal Vesicle) | | p |
|---|---|---|---|---|---|---|---|
| | | | mean | SD | mean | SD | |
| PTV | | | | | | | |
| | Dmax | Gy | 43.72 | 0.55 | 44.40 | 0.58 | <0.001 |
| | Coverage | > 95 % | 96.73 | 0.94 | 96.50 | 0.92 | 0.397 |
| | CI | ≤ 1.2 | 1.19 | 0.004 | 1.20 | 0.004 | 0.007 |
| | HI | ≤ 1.2 | 1.09 | 0.03 | 1.09 | 0.03 | 0.452 |
| | nCI | ≤ 1.2 | 1.12 | 0.03 | 1.13 | 0.04 | 0.225 |
| | MU | - | 33187.65 | 3127.09 | 35507.60 | 2250.67 | 0.019 |
| | Time | Minute | 29.40 | 1.32 | 30.55 | 0.55 | 0.022 |
| Bladder | | | | | | | |
| | Dmax | 39 Gy | 38.39 | 0.68 | 39.21 | 0.56 | <0.001 |
| | V37.5 | < 5 cm3 | 1.38 | 1.32 | 3.03 | 1.60 | <0.001 |
| | V37 | < 10 cm3 | 2.82 | 1.78 | 4.59 | 2.28 | <0.001 |
| | V18.125 | < 40 % | 28.78 | 15.13 | 35.25 | 20.85 | 0.007 |
| | D0.1cc | Gy | 38.12 | 0.61 | 38.71 | 0.75 | 0.004 |
| | D1cc | Gy | 37.40 | 0.61 | 38.03 | 0.66 | <0.001 |
| | D5cc | Gy | 35.94 | 1.28 | 36.56 | 0.99 | 0.001 |
| | D10cc | Gy | 31.84 | 6.63 | 33.12 | 5.90 | 0.001 |
| | D15cc | Gy | 30.10 | 4.11 | 31.82 | 3.05 | 0.003 |
| Rectum | | | | | | | |
| | Dmax | 39 Gy | 38.27 | 0.56 | 38.69 | 0.51 | <0.001 |
| | V36.25 | < 5 % | 0.88 | 0.55 | 2.35 | 2.91 | 0.042 |
| | V32.625 | < 10 % | 5.47 | 2.01 | 5.93 | 2.54 | 0.198 |
| | V29 | < 20 % | 10.78 | 2.99 | 12.26 | 3.41 | 0.001 |
| | V18.125 | < 50 % | 28.43 | 8.70 | 34.37 | 9.34 | <0.001 |
| | V5 | % | 68.59 | 17.61 | 74.69 | 16.34 | 0.001 |
| | V10 | % | 49.51 | 14.28 | 60.21 | 17.32 | <0.001 |
| | V20 | % | 25.61 | 5.97 | 29.81 | 8.32 | 0.010 |
| Penile Bulb | | | | | | | |
| | V29.5 | < 50 % | 16.30 | 23.67 | 18.64 | 22.93 | 0.037 |
| | V30 | < 3 cc | 1.41 | 3.33 | 1.48 | 3.34 | 0.131 |
| LFH | | | | | | | |
| | V14.5 | < 5 % | 0.09 | 0.22 | 0.12 | 0.31 | 0.180 |
| | Dmax | < 30 Gy | 13.50 | 1.79 | 13.89 | 1.68 | 0.209 |
| RFH | | | | | | | |
| | V14.5 | < 5 % | 1.06 | 1.66 | 0.63 | 1.32 | 0.398 |
| | Dmax | < 30 Gy | 15.12 | 1.66 | 15.25 | 1.58 | 0.746 |
| Neurovascular bundles | | | | | | | |
| | V37.5 | < 20 % | 2.11 | 2.83 | 4.18 | 3.20 | <0.001 |
| | V38 | < 50 % | 0.86 | 1.77 | 1.18 | 1.85 | 0.047 |
| Bowel | | | | | | | |
| | Dmax | 25 Gy | 15.25 | 7.55 | 16.45 | 8.00 | 0.053 |
| | V24 | < 1 cc | 0.05 | 0.13 | 0.75 | 2.23 | 0.068 |

CI: Conformity index; CTV: Clinical target volume; HI: Homogeneity index; LFH: Left femoral head; MU: Monitor unit; nCI: New conformity index; PTV: Planning target volume; RFH: Right femoral head; SD: Standard deviation

**Table 3.** Dosimetric comparisons of target volume and organs at risk doses for volume of PTV

| Structure | Dosimetric index | Plan 1 (Prostate) | | | | | Plan 2 (Prostate+Proximal Seminal Vesicle) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | PTV volume <100 cc | | PTV volume ≥100 cc | | p | PTV volume <100 cc | | PTV volume ≥100 cc | | p |
| | | mean | SD | mean | SD | | mean | SD | mean | SD | |
| PTV | | | | | | | | | | | |
| | Dmax | 43.44 | 0.45 | 44.13 | 0.42 | 0.003 | 44.14 | 0.70 | 44.53 | 0.47 | 0.149 |
| | Coverage | 97.07 | 0.95 | 96.20 | 0.67 | 0.039 | 96.62 | 1.13 | 96.43 | 0.83 | 0.659 |
| | CI | 1.19 | 0 | 1.19 | 0 | 0.165 | 1.2 | 0.01 | 1.2 | 0.00 | 0.180 |
| | HI | 1.08 | 0.01 | 1.08 | 0.04 | 0.094 | 1.1 | 0.04 | 1.08 | 0.03 | 0.393 |
| | nCI | 1.12 | 0.03 | 1.12 | 0.03 | 1.000 | 1.13 | 0.04 | 1.12 | 0.03 | 0.538 |
| | MU | 33127.58 | 3279.58 | 33277.75 | 3102.42 | 0.920 | 34206.85 | 2434.52 | 36208.23 | 1881.09 | 0.055 |
| | Time | 29.06 | 1.37 | 30 | 1.3 | 0.594 | 30.12 | 0.98 | 30.52 | 0.76 | 0.224 |
| Bladder | | | | | | | | | | | |
| | Dmax | 37.93 | 0.47 | 39.07 | 0.11 | <0.001 | 38.81 | 0.39 | 39.41 | 0.53 | 0.017 |
| | V37.5 | 0.56 | 0.71 | 2.45 | 1.18 | <0.001 | 1.69 | 1.42 | 3.57 | 1.37 | 0.001 |
| | V37 | 1.9 | 1.02 | 4.17 | 1.84 | 0.002 | 2.95 | 1.98 | 5.46 | 1.98 | 0.014 |
| | V18.125 | 24.6 | 15.06 | 35.05 | 13.77 | 0.134 | 22.17 | 4.87 | 42.28 | 22.87 | 0.036 |
| | D0.1cc | 37.70 | 0.39 | 38.72 | 0.23 | <0.001 | 38.32 | 0.42 | 38.91 | 0.82 | 0.095 |
| | D1cc | 37.06 | 0.58 | 37.88 | 0.13 | 0.001 | 37.54 | 0.48 | 38.29 | 0.61 | 0.012 |
| | D5cc | 35.54 | 1.37 | 36.57 | 0.87 | 0.087 | 35.82 | 1.23 | 36.94 | 0.57 | 0.001 |
| | D10cc | 32.65 | 3.07 | 31.61 | 10.08 | 0.514 | 32.88 | 2.39 | 33.23 | 7.23 | 0.011 |
| | D15cc | 28.62 | 4.11 | 32.31 | 3.15 | 0.046 | 29.72 | 3.25 | 32.94 | 2.36 | 0.020 |
| Rectum | | | | | | | | | | | |
| | Dmax | 38.26 | 0.59 | 38.27 | 0.55 | 0.975 | 38.57 | 0.64 | 38.74 | 0.44 | 0.479 |
| | V36.25 | 0.82 | 0.52 | 0.97 | 0.61 | 0.567 | 2.95 | 4.92 | 2.02 | 1.00 | 0.509 |
| | V32.625 | 5.02 | 2.21 | 6.12 | 1.56 | 0.241 | 5.24 | 2.79 | 6.3 | 2.43 | 0.390 |
| | V29 | 10.02 | 3.49 | 11.9 | 1.61 | 0.176 | 10.25 | 3.74 | 13.33 | 2.79 | 0.051 |
| | V18.125 | 26.66 | 10.26 | 31.07 | 5.19 | 0.279 | 29.21 | 10.81 | 37.13 | 7.48 | 0.069 |
| | V5 | 63.41 | 19.15 | 76.35 | 12.27 | 0.109 | 67.35 | 22.30 | 78.63 | 11.22 | 0.145 |
| | V10 | 45.86 | 15.58 | 54.97 | 10.74 | 0.168 | 54.14 | 22.79 | 63.46 | 13.50 | 0.252 |
| | V20 | 25 | 7.20 | 26.43 | 4.05 | 0.621 | 25.21 | 8.99 | 31.34 | 7.80 | 0.129 |
| Penile Bulb | | | | | | | | | | | |
| | V29.5 | 13.65 | 20.95 | 20.25 | 28.32 | 0.556 | 7.18 | 10.89 | 24.8 | 25.60 | 0.102 |
| | V30 | 1.03 | 2.43 | 1.96 | 4.49 | 0.555 | 1.54 | 3.20 | 1.44 | 3.55 | 0.953 |
| LFH | | | | | | | | | | | |
| | V14.5 | 0 | 0.00 | 0.21 | 0.32 | 0.031 | 0 | 0.00 | 0.17 | 0.37 | 0.233 |
| | Dmax | 13.16 | 1.47 | 14 | 2.20 | 0.321 | 12.5 | 1.12 | 14.63 | 1.46 | 0.003 |
| RFH | | | | | | | | | | | |
| | V14.5 | 0.21 | 0.58 | 2.32 | 1.97 | 0.002 | 0.04 | 0.11 | 0.94 | 1.56 | 0.149 |
| | Dmax | 14.45 | 1.47 | 16.12 | 1.46 | 0.022 | 14.1 | 0.64 | 15.86 | 1.61 | 0.013 |
| Neurovascular bundles | | | | | | | | | | | |
| | V37.5 | 2.85 | 3.44 | 0.98 | 0.89 | 0.153 | 4.21 | 2.70 | 4.16 | 3.55 | 0.973 |
| | V38 | 1.37 | 2.15 | 0.08 | 0.25 | 0.112 | 1.61 | 1.97 | 0.94 | 1.82 | 0.457 |
| Bowel | | | | | | | | | | | |
| | Dmax | 14.33 | 8.23 | 16.61 | 6.68 | 0.523 | 14.71 | 8.48 | 17.38 | 7.92 | 0.492 |
| | V24 | 0.05 | 0.12 | 0.05 | 0.14 | 0.891 | 0.67 | 1.78 | 0.79 | 2.53 | 0.913 |

CI: Conformity index; CTV: Clinical target volume; HI: Homogeneity index; LFH: Left femoral head; MU: Monitor unit; nCI: New conformity index; PTV: Planning target volume; RFH: Right femoral head; SD: Standard deviation

## DISCUSSION

Prostate SBRT for low-risk PCa is an evolving treatment modality with promising oncologic outcomes.[5-7] The safety and feasibility of SBRT has been demonstrated in the light of data accumulated over the years.[11,13,14] Unlike conventional RT, data on dosimetric constraints for SBRT to guide treatment planning for OARs are still insufficient. While SBRT studies determining long-term late toxicity data are still under investigation, clinicians should consider the doses delivered to OARs exposed during the SBRT treatment planning process.

In this dosimetric investigation, we evaluated the effect of inclusion of the proximal seminal vesicle in the target volume on the dose distribution of adjacent organs in low-risk PCa patients undergoing SBRT. It was determined that Dmax value and CI increased in terms of target parameters with the inclusion of the proximal seminal vesicle. In addition, due to the expansion of the target volume, a prolongation of the beam on time and an increase in MU were detected. There was an increase in the doses to which OAR was exposed, especially in the bladder and rectum. However, it was observed that these increases did not exceed the acceptable values according to the dose constraints used in our clinic, except for bladder and rectum Dmax values. Another important point to be emphasized is that in patients with a PTV volume above 100 cc, doses to which only the bladder was exposed were found to be significantly increased.

First of all, due to the near proximity of OARs to the target, the use of steep dose gradients, and organ mobility, the definition of the target and OARs volumes for prostate SBRT is crucial. The rectum and bladder are stretchable organs with significant intra- and inter-fraction variation potential. In order to prevent these situations, before the simulation, applications such as Foley catheterization into the bladder, filling the bladder, and bowel preparation with rectal enema, or the use of rectal balloon have been tried so far. Also, placement of hydrogel spacers between the rectum and the prostate to reduce rectal toxicity has also been investigated. In some studies, it is seen that hollow organs such as the bladder and rectum are contoured as a whole organ, while in others, the wall is contoured separately. In some SBRT studies, this information is not explicitly stated. Taking into account all of this information, each clinic establishes its own protocol and accepts patients. In our clinic, patients are simulated a comfortably full bladder and an empty rectum, in order to give SBRT safely and accurately. Fiducial markers are implanted 1 week prior to simulation for target tracking. During SBRT, 4 fiducial markers are also monitored. When the bladder is not full or the rectum is not empty as in simulation CT, it causes a decrease in the number of fiducial markers that can be monitored during treatment, and the treatment is interrupted until these conditions are corrected. Thus, accurate reproducibility of the treatment is ensured and the doses calculated in the planning for the OARs are not exceeded.

In general, both acute and late genitourinary (GU) toxicity are known to occur more frequently than gastrointestinal (GI) toxicity.[15-17] King et al.[18] evaluated both early and late expanded prostate cancer index composite-26 (EPIC-26) quality of life (QOL) outcomes based on various prospective SBRT trials including 864 patients. Within the first three months following SBRT, there was a brief deterioration in the urine and bowel domains, which improved or returned to baseline level within six months, and remained that way for at least five years. They reported that up to a 5-y observation period, prostate SBRT was well tolerated.

Various dosimetric parameters, including high doses delivered to even small volumes or low/moderate doses delivered to large volumes, and GU toxicity have also been linked in several studies.[19-22] Gomez et al.[19] reported the results of comparison of the EPIC-26 QOL changes and dosimetric parameters for 75 patients. They claimed that a high bladder V100% value and high PTV V100% higher than 120 cc were linked to decreased GU QOL. Similarly, in their study published in 2016, Qi et al.[20] found that these parameters correlate with GU toxicity. Seymour et al.[21] reported the toxicity assessment according to the International Prostate Symptom Scores (IPSS) in 56 patients who underwent SBRT. Baseline IPSS >7, prostate volume >50 cc, urethra V44, and bladder V19 values all increased the likelihood of any grade 2+ GU toxicity. Iarrobino et al.[22] evaluated the EPIC-26 scores of a total of 95 patients. Both late urinary incontinence and obstructive/irritative decreases were linked with higher bladder V37 (≥3.35 cc) values. In our study, bladder Dmax and V37 value increased from 38.39 Gy and 2.82 cc in the first plan to 39.21 Gy and 4.59 cc in the second plan. At the same time, we found a significant increase in the second plan with the expansion of the target volume in all the dosimetric variables we examined. As in the above-mentioned studies, since high doses to which the bladder is exposed are important in the development of GU toxicity, expansion of the target volume may cause an increase in GU toxicity. In addition, in our study, it was observed that the increased volume of PTV affected bladder doses, which was consistent with the literature. Regardless of the plan type, it was determined that the bladder received dosimetrically higher doses in the plans with a PTV volume above 100 cc.

Regarding GI toxicity, several studies have shown that various dosimetric parameters are associated with GI side effects.[19,22-24] According to Gomez et al.[19] patients with rectal V90 and V100 values >4.2 and >1.5 cc, respectively, had considerably lower bowel QOL. Iarrobino et al.[22] reported higher rectum V36 values (>0.58 cc) and D5% (33 Gy) that were correlated with EPIC declines at 6 months. In the study in which 259 patients from 18 centers were evaluated, a rectum Dmax value above 37.4 Gy was associated with a decrease in the EPIC-26 score.[23] The recently published analysis highlighted moderate doses delivered in large volumes into the rectum in 103 patients. In terms of patient-reported bowel QOL and physician-scored grade 2+ GI toxicity, respectively, rectum D19% and V20 values were linked to an increased likelihood of a clinically significant decline.[24] In our study, statistically significant differences were found in all dosimetric variables examined for the rectum as well as for the bladder. The mean rectum Dmax value increased from 38.27 Gy in the first plan to 38.69 Gy in the second plan. We could not make a comparison because we evaluated rectum V36 as % instead of cc.

Another OAR that we evaluated dosimetrically was the penile bulb. Evaluation with the EPIC-26 score can be confusing, since sexual function depends on many factors such as age, co-morbidity, and use of hormone therapy. This is why, unlike bladder and rectum EPIC-26 scores, worsening rather than improvement is encountered.[18,25] Penile bulb V29.5 <50% and V30 <3 cc were evaluated dosimetric parameters, however, no significant relationship could be demonstrated between erectile dysfunction and these values.[25,26] In our study, lower dosimetric values were found in both plans, but only the mean value of penile bulb V29.5 was significant in terms of exposure doses, with 16.30 in plan 1 and 18.64 in plan 2.

In addition, femoral heads, neurovascular bundles, and bowel were also evaluated dosimetrically. While there was no dosimetric difference for the femoral heads and bowel with the enlargement of the target volume, the neurovascular bundles V37.5 and V38 values increased.

This study had several potential limitations. Although our study was a relatively small number with low heterogeneity, the results were statistically significant. Since the study was a retrospective comparison study, the possibility of toxicity and its reflection on the clinic could not be evaluated.

## CONCLUSION

We evaluated the dosimetric differences that may occur in OARs by giving the same dose to two different target volumes. We chose the 5x7.25=36.25 Gy treatment scheme because it is now more safely preferred and its long results are better known. Numerous studies have demonstrated that the likelihood of developing GU and GI toxicity after prostate SBRT is associated with exposure of OARs to high doses delivered to small volumes. Therefore, increases in high dose volumes that may be considered quantitatively insignificant in routine clinical practice may be overlooked as they do not exceed dose restrictions and may possibly be important in the development of toxicity. As there are no clear guidelines on when to include the proximal seminal vesicle to the target volume in low-risk PCa, we recommend that special attention be paid to the high doses exposed in OARs in this patient group. In addition, it should be kept in mind that bladder toxicity may increase with increasing PTV volume, especially above 100 cc.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Samsun University Clinical Researches Ethics Committee (Date: 2023, Decision No:06/10)

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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